REMARKS

Claims 1-23 were filed in the original case. Claims 1-23 were cancelled and Claims 24-44 were added in a previous amendment. Claims 24-44 were cancelled and Claims 45-71 were added in a previous amendment. Claims 69 and 70 are cancelled in the present amendment. These cancellations are made without acquiescing to the Examiner's rejections, but are made to further prosecution and Applicant's business interests. Applicant reserves the right to prosecute Claims 69 and 70 (or similar claims) in the future. Claims 45-48 and 71 are presently amended. Therefore, Claims 45-68 and 71 are currently pending.

In the Office Action dated July 8, 2003 the Examiner has made three rejections. The currently pending rejections are:

1) Claims 46-48, 71 stand rejected under 35 U.S.C. 112, first paragraph;
2) Claims 45-68, 71 stand rejected under 35 U.S.C. 112, second paragraph; and
3) Claims 45, 48-68, 71 stand rejected under 35 U.S.C. 102(b) in view of:
    a) 1997 Boehringer Mannheim Biochemicals Catalog.
    b) 1996 Perkin Elmer, PCR Systems, Reagents & Consumables catalog.
    c) 1993 Applied Biosystems Catalog.

Applicant believes that the pending Claims are fully supported, are definite, and are not taught by the prior art. Therefore Claims 45-68, 71 should be passed into allowance.

REJECTIONS

For clarity, the rejections at issue are set forth by number in the order they are herein addressed.

I. THE SPECIFICATION FULLY SUPPORTS THE CLAIMS

In the Final Office Action of July 8, 2003, the Examiner has rejected Claims 46-48, and 71 under 35 U.S.C. 112, first paragraph:

"Claims 46-48, 71 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amendment fails to point to any support in the specification for the newly added language. However, the specification does not appear to describe or discuss "a computer readable medium" and a "decision tree". The concept of "a computer readable medium" and a "decision tree" does not appear to be part of the originally filed invention. Therefore "a computer readable medium" and a "decision "tree" constitutes new matter. Applicant is required to cancel the new matter in reply to this office action." (Final Office Action July 8, 2003, page 3.) (Emphasis added.)

Applicant respectfully disagrees. To the contrary, the Specification provides ample, specific and detailed support for the Claims. Several non-limiting examples directly quoted from the Specification are provided:

"Assays for detection of polymorphisms or mutations fall into several categories, including, but not limited to direct sequencing assays, fragment polymorphism assays, hybridization assays, and **computer based data analysis."** (Specification, II. "Assays for Generating Genomic Profiles", page 40. Emphasis added.)

"In some embodiments of the present invention, **perioperative genomic profiles are generated using computer-based data analysis** of a genetic information sample (e.g., stored nucleic acid sequence information). A sample is collected from a subject at anytime (e.g., at birth), sequence information is generated (e.g., through DNA sequencing), and **the information is stored (e.g., as digital information on a portable chip).** During the perioperative period, the subject's sequence information is **scanned by a computer program** for the pre-selected markers. A report (e.g., a perioperative genomic profile) is generated." (Specification II.E., "**Computer-Based Data Analysis**", page 49. Emphasis added.)

"In some embodiments of the present invention, **the data is generated, processed, and/or managed using electronic communications systems** (e.g., Internet-

based methods). In some embodiments, **a computer-based analysis program is used to translate the raw data** generated by the genomic profile (e.g., the presence or absence of a given SNP or mutation) **into data of predictive value for the clinician** (e.g., probability of abnormal pharmacological response, presence of underlying disease, or differential diagnosis of known disease)." (Specification, III. "Analysis and Delivery of Data", page 50. Emphasis added.)

"Where the sample comprises previously determined genetic information (e.g., sequence information, SNP or mutation information, etc.), the information may be directly sent to the genomic profiling service by the subject (e.g., a information card containing the genetic information may be **scanned by a computer and the data transmitted to a computer** of the genomic profiling center using an electronic communication systems). Once received by the genomic profiling service, the sample is processed and a genomic profile is produced (i.e., genomic data), specific for the medical or surgical procedure the subject will undergo." (Specification, III. "Analysis and Delivery of Data", pages 50-51. Emphasis added.)

"In some embodiments, the process of selecting markers, **performing detection assays,** and distributing data to subjects and clinicians is organized by **an integrated electronic (e.g., web-based) system.**" (Specification, "Detailed Description of the Invention", page 30. Emphasis added.)

"The present invention contemplates **any method capable of receiving, processing, and transmitting the information to and from medical personal and subject.**" (Specification III., "Analysis and Delivery of Data", page 50. Emphasis added.)

"In some preferred embodiments of the present invention, the information generated by perioperative **genomic profiling is distributed in a coordinated and automated fashion.**" (Specification III. "Analysis and Delivery of Data, page 49. Emphasis added.)

"The fate of the sample and genomic data is driven by the subject, who is given a **menu (e.g. electronically) of choices**. . . . For example, using an **electronic communication system**, the central facility can provide data to the clinician, the subject, or researchers. . . . In some embodiments, the subject may be able to directly access the

data using the **electronic communication system."** (Specification III. "Analysis and Delivery of Data, page 51. Emphasis added.)

"The data may be displayed to the clinician by any suitable method. For example, in some embodiments, the genomic profiling service generates a report that can be printed for the clinician (e.g., at the point of care) or **displayed to the clinician on a computer monitor**." (Specification III., "Analysis and Delivery of Data", page 51. Emphasis added.)

"The data generated by the assay may converted to **a genomic profile in a computer system** of the emergency vehicle or may be **transmitted to distant computer system for processing**." (Specification III., "Analysis and Delivery of Data, page 51. Emphasis added.)

In order to further the prosecution of the present case, while not acquiescing to the Examiner's argument, and retaining the right to prosecute the original claims (or similar claims) in the future, Applicant has amended Claims 46-48 and 71 to recite "computer program" and "information to optimize perioperative care".

In view of the above, Applicant requests that the Examiner withdraw this rejection and enter the amendments, as there appears to be no issue on this point when the amendments are entered.

II. THE CLAIMS ARE DEFINITE

In the Final Office Action of July 8, 2003 the Examiner has rejected Claims 45-68 and 71 under 35 U.S.C. 112, second paragraph:

> "Claims 45-68, 71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention."
>
> "The response asserts that the claimed reagents provide agents for detecting the variant alleles using the range of different technologies described in the specification." This argument has been thoroughly reviewed, but is not found persuasive because the claim does not require that the reagents in fact detect the

presence of the variant alleles. The claim could be amended to recited "reagents which detect . . ." to overcome the rejections." (Page 4.) (Emphasis added.)

Applicant respectfully disagrees. However, in order to further the prosecution of the present case, while not acquiescing to the Examiner's argument, and retaining the right to prosecute the original claims (or similar claims) in the future, Applicant has amended Claims 45 and 71 **as suggested by the Examiner** to recite "reagents which detect . . .", and "component parts which detect . . .", respectively.

In view of the above, Applicant requests that the Examiner withdraw this rejection and enter the amendments, as there appears to be no issue when the amendments are entered.

IV. THE CITED REFERENCES DO NOT ANTICIPATE THE CLAIMS

In the Final Office Action of July 8, 2003, the Examiner has rejected Claims 45, 48-68, and 71 under 35 U.S.C. 102(b) as being anticipated by the catalogs of three manufacturers: Boehringer Mannheim; Perkin Elmer; and Applied Biosystems. For clarity and efficiency, because their defects as prior art are shared, and because the Examiner has cut and pasted verbatim from the Boehringer Mannheim text of the Final Office Action of July 8, 2003 to the Perkin Elmer and Applied Biosystems texts of the Final Office Action of July 8, 2003 (without even changing "Boehringer Mannheim" to "Perkin Elmer" (page 12) or "Applied Biosystems" (page 17)), the three references will be addressed together.

The text of 35 U.S.C. 102 quoted by the Examiner reads:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application in the United States.

(Final Office Action July 8, 2003, page 5).

Applicant respectfully asserts that the references cited by the Examiner glaringly fail to meet this standard of anticipation. To the contrary, the catalog pages **do not teach** a perioperative genomic profile kit. The catalog pages **do not teach** reagents which detect the presence of variant alleles of two or more genes selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNF*α and *TNF*β. The catalog pages **do not teach** instructions for using a kit for generating a perioperative genomic profile for a subject. The catalog pages **do not teach** computer programs or information stored in a memeory to optimize perioperative care. The prior art references **do not teach** a kit having components that provide a subject-specific clinical pathway of medical intervention if used.

Applicant reminds the Examiner that the Federal Circuit has stated the relevant analysis for anticipation as follows:

> "A claim is anticipated only if each and every element as set forth in the claims is found, either expressly or inherently described, in a single prior art reference."[1]

Applicant respectfully submits that not one of the catalog references cited by the Examiner teach each and every element as set forth in the claims.

In view of the above, Applicant requests that these rejections be withdrawn.

A. The Claims Require Detection of Specific Variant Alleles - The Examiner's Cited Catalog Pages Do Not Teach this Element

In the Applicant's Amendment and Response to Office Action Dated January 21, 2003 (filed April 14, 2003), Applicant pointed out to the Examiner that:

> "None of the three references teaches variant alleles of the genes of the present invention. None of the three references teaches detection of variant alleles in two or more genes from the group of genes of the present invention." (Amendment and Response to Office Action of January 21, 2003, filed April 14, 2003, page 9).

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[1] *Verdegaal Bros. V. Union Oil of California*, 2 USPQ2d 1051, 1053 (Fed.Cir. 1987)

In the Final Office Action of July 8, 2003 the Examiner argues:

> "This argument has been thoroughly reviewed, but is not found persuasive because the claim does not require detection of the variant alleles." (Final Office Action July 8, 2003, page 8).

Applicant respectfully disagrees. To the contrary, the catalog pages cited by the Examiner have no teaching or suggestion to use variant alleles of two or more of the claimed genes. Thus, none of the Examiner's cited references teach or suggest kits having reagents capable of detecting the specific variant alleles as recited in the claims. Hence, the Examiner has not responded to the main point of Applicant's rebuttal.

However, in order to further the prosecution of the present case, while not acquiescing to the Examiner's argument, and retaining the right to prosecute the original claims (or similar claims) in the future, Applicant has amended Claims 45 and 71 **as suggested by the Examiner** to recite "reagents which detect . . .", and "component parts which detect . . .", respectively.

In view of the above, Applicant requests that the Examiner withdraw this rejection and enter the amendments, as the prior art fails to teach the elements of either the original claims or the amended claims, and there is no issue when the amendments are entered.

B. Instructions are Functional Components of the Claimed Kits and Cannot be Ignored

In the Final Office Action of July 8, 2003 the Examiner has rejected Claims 45, 48-68, and 71 under 35 U.S.C. 102(b) as being anticipated by the catalogs of three manufacturers: Boehringer Mannheim; Perkin Elmer; and Applied Biosystems. Not one of the three prior art references recite the limitation "instructions for using said kit for generating said perioperative genomic profile for said subject." as recited in Claim 45 of the present invention. Nevertheless, the Examiner persists in repeating a rejection under

35 U.S.C. 102(b) only by improperly ignoring this element. (Final Office Action July 8, page 8).

1. The Examiner's Rejection of Instructions as Functional Components of the Claimed Kits is Procedurally and Statutorily Defective

The Examiner has **never** argued in the Office Action of December 2, 2002, in the Office Action of January 21, 2003, in the Final Office Action of July 8, 2003, or in the Advisory Action of October 16, 2003 that the Examiner's cited catalog references teach instructions for the operation of a perioperative genomic profiling kit. Because the prior art fails to teach each and every limitation of the claims, the Examiner's argument that the cited art references anticipate the present invention under 35 U.S.C, 102(b) is procedurally and statutorily defective, and must be withdrawn.

Rather, the Examiner argues whether instructions for generating a perioperative genomic profile are a legitimate claim element, not whether instructions for the operation of the kit are anticipated by the Examiner's references (i.e., under 35 U.S.C, 102(b). (Final Office Action of July 8, 2003, pages 9-11.) Clearly, instructions of the present invention are a legitimate claim element, and there is no question that the prior art cited by the Examiner fails to teach or suggest the limitation of instructions for using the kits of the present invention for generating a perioperative genomic profile for a subject. Nor has the Examiner asserted otherwise. Therefore, 35 U.S.C, 102(b) is satisfied, there is no statutory basis for the Examiner's rejection, and the claims must be passed into allowance.

2. The Examiner Confuses Instructions for the Operation of a Kit with a "Statement of Intended Use" and Has Failed to Properly Respond to Applicant's Response

In the Advisory Action of October 16, 2003 the Examiner argues:

> "The response asserts that the intended use which is recited on the instructions with printed instructions for use. (sic) This argument has been thoroughly addressed in the final rejection." (Page 3).

Because of the grammatical error, Applicant does not understand the Examiner's position. Applicant therefore assumes that the Examiner is reiterating the same arguments as those to be found in the Final Office Action of July 8, 2003 (pages 9-11) in which the Examiner confuses **instructions for the operation of a kit** with a **statement of intended use**. For example, the Examiner argues:

> "The intended use which is recited on the instructions lacks a functional relationship to the kit because the instructions do not physically or chemically affect the chemical nature of the components of the kit, and furthermore, the components of the kit can still be used by the skilled artisan for other purposes (as a whole or individually). (Office Action 7/8/2003, page 10).

If this is in fact what the Examiner has meant in the Advisory Action of October 16, 2003, then the Applicant's argument has **not** been thoroughly addressed in the Applicant's Amendment and Response to the Office Action of January 21, 2003, **or even addressed at all** in the Applicant's Amendment and Response to Final Office Action Dated July 8, 2003, originally filed September 8, 2003.

For example, in the Final Office Action of July 8, 2003, the Examiner argues:

> "In re Haller states that, in accordance with the patent statutes, an article or composition of matter, in order to be patentable, must not only be useful but must be new. *If there is no novelty in an article or composition itself, then a patent cannot be properly granted on the article or composition regardless of the use for which it is intended.*" (Final Office Action July 8, 2003, page 9. Italics in original. Underline added.)

However, *In re Haller* is of **no relevance** to rejection of the present invention. Instructions are not a "statement of intended use", nor are instructions "mere re-labelling" (*In re Haller*, 403). In citing *In re Haller*, the Examiner mistakenly confuses operational kit instructions with "an admittedly old compound, labelled for a new use as an

insecticide", (*id* at 403), while *In re Haller* itself does not make the Examiner's mistake. Indeed, the term "instructions" and "kit" fail to appear anywhere in the text of *In re Haller*.

In the Amendment and Response to Office Action of January 21, 2003, Applicant pointed out to the Examiner that the **claimed instructions** are **novel, physical components** dictating the **manipulations of physical objects and activities** which, as components of the claimed kits, **implement a set of actions to accomplish a useful, concrete and tangible result**. (Amendment and Response to Office Action of January 21, 2003, Page 11.) Under some embodiments of the present invention, instructions that direct, for example, a treatment course of action utilize **physically organized data structures** for two or more assays, which are not fixed or determinate beforehand. A patient's preferred clinical pathway cannot properly be executed in advance absent the results of the assay as instructed. **Instructions that cause and direct a particular treatment course of action** utilize results from two or more genotypes. A combination of markers may well instruct one course of action rather than another.

In the Final Office Action of July 8, 2003, and in the Advisory Action of October 16, 2003, the Examiner has conspicuously failed to respond to these factual assertions. Indeed, the Examiner concedes in the Final Office Action of July 8, 2003 that:

> "The instructions are used to describe how the kit is intended to be used."
> (Final Office Action of July 8, 2003, page 9. Emphasis added).

Nevertheless, in the Final Office Action of July 8, 2003 and the Advisory Action of October 16, 2003 the Examiner continues to confuse *In re Haller's* "the use for which it is intended" (i.e. a statement of the kit's **purpose**), with "**how** the kit is intended to be used", i.e. the claimed and patentable instructions for **operation** of the present invention that **embody functional components, interacting with other components** of the claimed kits, in **novel modes of cooperation,** thereby **permitting the kit's functionality to be realized**. (Amendment and Response to Office Action January 21, 2003, page 11.)

The instructions of Claims 45 - 68 are physical component parts of the Claims. For example, a claim to "A system of doing X, comprising component Y" is anticipated

by prior art that discloses component Y for purposes other than X (i.e., use X is a statement of use the does not impart patentable weight to the claim). However, a claim that recites "A system comprising component Y and component Z, wherein component Z is configured to permit component Y to find use in process X" is patentable if the prior art does not teach the use of component Y in process X, or does not teach the use of component Z that is configured to facilitate the use of Y for X. The present claims represent the latter rather than the former example.

Contrary to thoroughly addressing these facts, the Examiner has been mute in response. In view of the above, Applicant requests that the Examiner respond to the Applicant's rebuttal, or withdraw the rejections.

3. The Examiner has Improperly Applied the Law of *In re Gulack,* Which Stands for the Patentability of the Present Invention

In the Advisory Action of October 16, 2003 the Examiner argues:

> "Fourth, the response again asserts there is no case law or MPEP citation which is relevant such that the examiner has made up and does not comport with the law. Applicant is respectfully requested to read in re Gulack."

In re Gulack was provided by the Applicant to the Examiner in support of the assertion that ". . . printed matter, in an article of manufacture claim, *can* be given "patentable weight."[2] (Original emphasis.) The CAFC in *In re Levin* holds:

> "The only requirement that 35 U.S.C. §101 imposes as set forth in *In re Miller* is that a new and unobvious functional relationship must exist between the claimed combination of printed matter and other claimed elements. 418 F.2d at 1396, 164 U.W.P.Q. (BNA) at 49. For instance, as we have stated in In re Gulack, "the critical question is whether there exists any new and unobvious functional

[2] *In re Miller* 57 C.C.P.A. 809; 418 F.2d 1392.

relationship between the printed matter and the substrate." 703 F.2d at 1386, 217 U.S.P.Q. (BNA) at 404.[3]

Because novel, unobvious functional relationships clearly exist between the claimed instructions and substrate kits of the present invention, the present invention easily surmounts the requirements of the *In re Gulack* test. An instruction is "An authoritative direction to be obeyed; an order"; instructions are "Detailed directions on procedure." (The American Heritage Dictionary 3rd Edition, 1993). Clearly instructions do **not** "merely represent a statement of intended use" as the Examiner mistakenly alleges (Office Action of January 21, 2003, page 3). Hence, *In re Gulack* stands for exactly the opposite of the Examiner's conclusory and unsupported assertion.

In the Final Office Action of July 8, 2003 the Examiner argues:

> "However, in the case of *In re Gulack*, the printed matter is considered a patentable distinction because the function of the device depends upon the printed matter itself, which is a part of the substrate; without the printed indicia or numbers, the substrates lose their function. Such is not the case with the instantly claimed kit. The components of the kit remain fully functional absent the printed instructions for use." (Final Office Action July 8, 2003, page 9) (Emphasis added.)

The Examiner is wrong. As in *In re Gulack*, the printed matter instructions and reagents of the present invention are interrelated, so as to produce a new product useful for the medical purpose of generating a perioperative genomic profile for a subject. Although not required under the correct legal standard, in the present invention printed matter does not achieve its medical purpose of generating a perioperative genomic profile without the reagents, and the reagents of the present invention do not produce the desired result without the printed matter instructions (see the Declaration of Dr. Morris Waxler, and Section **B.4.** of the present Response to Office Action below). A kit for generating a perioperative genomic profile for a subject is a **previously unknown product**. Because

[3] *In re Levin*, 107 F.3d 30 (Fed. Cir. 1997).

the printed matter instructions are: 1) functionally related; 2) to a previously unknown product, the Applicant is entitled to the Claims.

The Examiner's mischaracterizations of the present invention's Claims are erroneous, and unsupported by any evidence, affidavit or other authority. To the contrary, the claimed instructions of the present invention clearly result in a structural and manipulative differences (*In re Casey*) between the manufacturer's catalogs cited by the Examiner as prior art, and the articles and compositions of the present claims. Rather than remaining fully functional, the **useful, concrete** and **tangible aspects of the kits** of the present claims are **not** maintained after removal of "printed instructions for use" (see the Declaration of Dr. Morris Waxler).

In turn, the Examiner's argument, raised for the first time in the Final Office Action of July 8, 2003, that "The components of the kit remain fully functional absent the printed instructions for use." represents a rejection that is unsupported by fact, evidence or law.

4. Dr. Morris Waxler's Declaration Is Evidence of a Functional Relationship Between Operational Instructions and the Perioperative Genomic Profile Kits of the Present Invention

The Examiner's unsupported statement that "the kit is unpatentable over the prior art because they function equally effectively with or without the instructions" is clearly erroneous. The Examiner repeats the identical mistake a second time in consideration of *In re Miller* stating:

> "no functional relationship exists between the instructions and the other elements of the kit because the components of the kit are capable of functioning without the printed matter." (Final Office Action of July 8, 2003, page 10)
>
> And:
>
> "the kit is unpatentable over the prior art because they function equally effectively with or without instructions, and accordingly no functional relationship exists

between the instructions for use and kit components." (Final Office Action of July 8, 2003 page 10).

Applicant submits herewith a Declaration of Morris Waxler, Ph.D. The Declaration explains that instructions for the use of an *in vitro* genetic diagnostic kit bear a critical functional relationship to the components of the kit, and that the function of an *in vitro* genetic diagnostic kit depends on the instructions. For example, without instructions approved by the Food & Drug Administration, the *in vitro* diagnostic kit is not considered functional by the Food & Drug Administration.

As evidenced by the Declaration of Morris Waxler, Ph.D. instructions for the use of an *in vitro* genetic diagnostic kit bear a **critical functional relationship** to the components of the kit, and that the function of an *in vitro* genetic diagnostic kit depends on the instructions. Dr. Waxler explains:

> "The function of an *in vitro* genetic diagnostic kit depends on the instructions to be approved by the Food &Drug Administration; without instructions the *in vitro* genetic diagnostic kit is not considered to be functional by the Food & Drug Administration."
>
> "an *in vitro* genetic diagnostic kit does not, and cannot, function equally effectively with or without instructions."
>
> "The functional relationship between an *in vitro* genetic diagnostic kit and its operation is critical such that component instructions must undergo rigorous Food & Drug Administration scrutiny before the kit may be manufactured or marketed in order to assure its safety, efficacy and reliability."
>
> "Without Food & Drug Administration approved instructions for its operation an *in vitro* genetic diagnostic kit cannot be manufactured or marketed." (Declaration of Morris Waxler, Ph.D. under 37 CFR §1.132, page 1)

Contrary to the Examiner's unsupported assertions, the Food & Drug Administration recognizes the importance of the instructions to enable use of the reagents, and use of data obtained by use of the reagents in the hands of practitioners.

To sustain the rejection, the Examiner must present **evidence** (not conclusory statements or guesses) as to the lack of a functional relationship between the claimed instructions and other components of the kits. The Examiner's rejection standing alone is not evidence. To the contrary, the Declaration of Dr. Waxler is objective factual evidence. The Examiner is not in possession of countervailing factual evidence.

Nor has the Examiner cited authority for the Examiner's proposition that the test for the presence or absence of a functional relationship is whether or not the components of the kit are capable of functioning without the printed matter. This is made-up law. The Examiner's unsupported assertion does not reflect the holding of *In re Miller*. The Examiner's unsupported assertion does not reflect the actual law. To the contrary, in *In re Miller* markings on a measuring cup are held to be patentable even though the cup is useful as a measuring cup without the markings.[4]

Therefore, Applicant requests the Examiner to consider the Declaration of Morris Waxler, PhD, and to withdraw the rejections.

5. The Examiner's "Physically or Chemically Affect the Chemical Nature" Standard is not the Law under 35 U.S.C. 102(b)

In the Advisory Action of October 16, 2003 the Examiner argues:

> "The third reason the response traverses is that the instructions both chemically and physically affect the chemical nature of the components of the kit. The final rejection has thoroughly responded to this arguments". (Page 3.)

To the contrary the Examiner hasn't responded to the Applicant thoroughly, or at all.

In the Final Office Action of July 8, 2003 the Examiner argues:

> "The intended use which is recited on the instructions lacks a functional relationship to the kit because the instructions do not physically or chemically affect the chemical nature of the components of the kit, and furthermore, the

[4] *In re* Miller, 418 F.2d 1392, 164 USPQ 46 (C.C.P.A. 1969).

components of the kit can still be used by the skilled artisan for other purposes (as a whole or individually). (Final Office Action July 8, 2003, page 10). (Emphasis added.)

In this assertion the Examiner makes **numerous errors** of both fact and law. First, the Examiner's arguments are conclusory, and unsupported by any citation to relevant case law, the MPEP, an affidavit, or other authority. Second, the Examiner confuses the "intended use which is recited on the instructions" with "printed instructions for use". Indeed, the Examiner tacitly acknowledges the difference in distinguishing "**intended use** which is recited **on** the instructions", from the body (how to) of the instructions. The claimed instructions of the present invention are not a "statement of intended use" (see above). Third, abundant examples are proffered in the Specification of the present invention of **instructions which both chemically and physically** affect the chemical nature of the components of the kit (See Section I.B. "Criteria for Selection of Markers", page 32, Section I.C. "Categories of Markers", page 34, Experimental Example 1 "Perioperative Genomic Screening for Anesthesia Markers", page 53, Experimental Example 2 "Generation of Genomic Profiles", page 57).

Fourth, the Examiner puts forward no relevant case law, MPEP citation, affidavit or other authority in which the legal test for a functional relationship rests on whether operational instructions "physically or chemically affect the chemical nature of the components of the kit." (Final Office Action July 8, 2003, page 10). This is a non-legal standard the Examiner has made up, and does not comport with the law.

6. The Examiner's "Use for Other Purposes" Standard is not the law under 35 U.S.C. 102(b)

The Examiner argues:

"The intended use which is recited on the instructions lacks a functional relationship to the kit because the instructions do not physically or chemically affect the chemical nature of the components of the kit, and furthermore, the components of the kit can still be used by the skilled artisan for other purposes (as

a whole or individually). Therefore the kit is unpatentable over the prior art . . ." (Office Action 7/8/2003, page 10). (Emphasis added.)

Applicant asserts that whether or not "the components of the kit can still **be used by the skilled artisan for other purposes** (as a whole or individually)" has no legal bearing on patentability. To reach this peculiar and erroneous standard the Examiner has misinterpreted the Examiner's own quoted law. For example, the Examiner argues:

> "Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In re Casey 370 F.2d 576, 152, USPQ 235 (CCPA 1967); In re Otto, 312 F.2d 937, 938 136 USPQ 458, 459, (CCPA 1963). (Final Office Action of July 8, 2003, page 9)

Nothing in the Examiner's cited case law, or any other case law, elucidates a standard that "use for other purposes" defines improper functional language. As detailed above, instructions for the operation of a genomic profiling kit are **not** a "statement (or recitation) of intended use" as mischaracterized by the Examiner, regardless of whether the reagents have additional potential uses. In the Advisory Action of October 16, 2003, the Examiner argues:

> "The response argues that the claims are not anticipated. The response asserts the examiners arguments are conclusory and unsupported by case law or the MPEP. The rejection of record cites both MPEP and case law on number of occasions (see pages 9-11, for example)." (Page 3.)

Applicant submits that the Examiner has misinterpreted the proper standard established by the MPEP and case law which - when considered - stands for the patentability of the present invention. Moreover, the Examiner impermissibly attempts to create a new non-legal standard, (i.e. whether "the components of the kit can be used by the skilled artisan for other purposes (wholly or individually)"). In view of the above, Applicant requests that the Examiner withdraw this rejection.

7. The Examiner has Improperly Ignored Applicant's Arguments Showing Distinguishing Features Between the Claims and the Prior Art

In the Final Office Action of July 8, 2003 the Examiner argues:

> "Applicant's arguments fail to comply with 37 CFR 1.111(b) because they amount to a general allegation that the claims define a patentable invention without specifically pointing out how the language of the claims patentably distinguishes them from the references." (page 11).

The Examiner has erred. To the contrary, in the Amendment and Response to Office Action Dated January 21, 2003 (filed April 14, 2003), the Applicant **expressly and specifically** responded to the Examiner:

> "**None of the three references teaches** variant alleles of the genes of the present invention. **None of the three references teaches** detection of variant alleles in two or more genes from the group of genes of the present invention. **None of the three references teaches** categorical criteria for the selection of genes and variant alleles of the present invention. **None of the three references teaches** generation of a perioperative genomic profile." (page 9).

Having clearly answered the Examiner's request to specifically point out how the language of the claims patentably distinguishes the claims from the references, Applicant respectfully requests that the Examiner withdraw this rejection under 35 USC §102(b).

For the numerous reasons cited above, the Examiner has improperly failed to consider the claim element of "instructions for using said kit for generating said perioperative genomic profile for said subject" in the claims. There is no dispute whatsoever that this claim element is not found in the prior art. Because this element must be considered, for at least the reasons recited above, the rejections must be withdrawn and the claims passed to allowance.

V. THE EXAMINER HAS IMPROPERLY EXAMINED CLAIM 71

The Examiner has failed to properly address the patentability of Claim 71. In particular, the Examiner rejects Claim 71 on grounds that are irrelevant to the claim.

In the Final Office Action of July 8, 2003 the Examiner has rejected Claim 71 under 35 U.S.C. 102(b) as being anticipated by the catalogs of three manufacturers: Boehringer Mannheim; Perkin Elmer; and Applied Biosystems. **Not one of the three prior art references recites** a perioperative genomic profile kit having component parts which detect the presence of variant alleles of two or more genes selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNF*α and *TNF*β. **Not one of the three prior art references recites** a genomic profiling kit comprising information to optimize perioperative care that, based at least on the presence or absence of variant alleles of two or more genes selected from the group consisting of *BChE, CYP2D6, F5, F2, CACNAIS, MTHFR, MTR, MTRR, CBS, TNF*α and *TNF*β measured by said kit, directs a user to a specific clinical pathway of medical intervention for said subject, as recited in Claim 71. Nevertheless, the Examiner persists in re-asserting a rejection under 35 U.S.C. 102(b) only by **improperly ignoring the absence of these limitations in the catalogs cited as prior art references**. (Final Office Action July 8, page 8).

Although the Examiner groups rejection of Claim 71 with rejections of Claims 45, and 48-68 in consideration of "arguments directed to instructions" (Final Office Action of July 8, 2003, page 8), **instructions for the operation of perioperative genomic profiling kits are not an element** of Claim 71. In lumping Claim 71 with the other rejections, the Examiner has entirely ignored claim elements unique to Claim 71. Thus, the Examiner has never addressed the subject matter of Claim 71. Because the Examiner

has failed to properly address the claim, Claim 71 must either be passed to allowance or a non-final office action must be issued on Claim 71.

E. CONCLUSION

It is respectfully submitted that Applicant's claims as amended should be passed into allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

Dated: 6/30/04

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PATENT
Attorney Docket No. **HOGAN-06650**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of :	Kirk Hogan	
Serial No.:	09/976,423	Group No.: 1634
Filed:	10/21/2001	Examiner: J.A. Goldberg
Entitled:	Methods and Compositions for Perioperative Genomic Profiling	

DECLARATION OF MORRIS WAXLER, Ph.D. UNDER 37 CFR §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF MAILING UNDER 37 C.F.R. 1.8(a)(1)(i)(B)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being sent by facsimile transmission to the U.S. Patent and Trademark Office, via Examiner J.E. Goldberg at (703) 746-5149.

Dated: 9-8-03 By: Mary Ellen Waite
Mary Ellen Waite

Madam:

1. I, Morris Waxler, am a specialist in Food & Drug Administration regulatory affairs at the law firm of LaFollette, Godfrey & Kahn.

2. As a Branch Chief at the Center for Devices and Radiological Health of the Food & Drug Administration for 26 years, I am knowledgeable about Food & Drug Administration requirements for the manufacture and marketing of approved medical devices and diagnostic kits.

3. Instructions for the use of an *in vitro* genetic diagnostic kit bear a critical functional relationship to other components of the kit.

4. The function of an *in vitro* genetic diagnostic kit depends on the instructions to be approved by the Food &Drug Administration; without instructions the *in vitro* genetic diagnostic kit is not considered to be functional by the Food & Drug Administration.

5. Therefore an *in vitro* genetic diagnostic kit does not, and cannot, function equally effectively with or without instructions.

6. The functional relationship between an *in vitro* genetic diagnostic kit and its operation is critical such that component instructions must undergo rigorous Food & Drug Administration scrutiny before the kit may be manufactured or marketed in order to assure its safety, efficacy and reliability.

7. Without Food & Drug Administration approved instructions for its operation an *in vitro* genetic diagnostic kit cannot be manufactured or marketed.

The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Dated: September 7, 2003 Signed: Morris Waxler

Morris Waxler, Ph.D.